L7 ANSWER 14 OF 112 MEDLINE
AN 94237211 MEDLINE
DN 94237211 PubMed ID: 8181520
TI Selective stimulation of murine cytotoxic T cell and antibody responses by particulate or monomeric hepatitis B virus surface (S) antigen.
AU Schirmbeck R; Melber K; Mertens T; Reimann J
CS Department of Bacteriology, University of Ulm, FRG.
SO EUROPEAN JOURNAL OF IMMUNOLOGY, (1994 May) 24 (5) 1088-96.
Journal code: EN5; 1273201. ISSN: 0014-2980.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199406
ED Entered STN: 19940621
Last Updated on STN: 19970203
Entered Medline: 19940614
AB In the murine system, we tested in **vivo** the immunogenicity of different preparations of the yeast-derived surface antigen (S-antigen or S-**protein**) of hepatitis B virus (HBV). Native S-**protein** molecules self-assemble into stable 22-nm particles. BALB/c mice immunized with low doses of native S-particles without adjuvants efficiently **generated** an H-2 class I-restricted CD8+ cytotoxic T lymphocyte (**CTL**) response, and developed easily detectable serum antibody titers against conformational determinants of the native S-particle or linear epitopes of the denatured S-**protein**. Disruption of S-particles with sodium dodecyl sulfate and beta-2-mercaptoethanol **generated** p24 S-monomers. Injection of an equal dose of S-monomers into mice efficiently primed **CTL**, but did not stimulate an antibody response against conformational or linear epitopes of the native or denatured S-**protein**. In **vivo** priming of **CTL** by S-particles or S-monomers required "endogenous" processing of the antigen because the injection of an equimolar (or higher) dose of an antigenic, S-derived 12-mer peptide into mice did not prime **CTL**. Native (particulate) or denatured (monomeric) S-antigen injected with mineral oil (incomplete Freund's adjuvant) or aluminum hydroxide failed to stimulate a **CTL** response. Hence, different preparations can be produced from a small **protein** antigen which specifically stimulate selected compartments of the immune system.
CT Check Tags: Animal; Comparative Study; Female; Male; Support, Non-U.S. Gov't
Amino Acid Sequence
Cytotoxicity Tests, Immunologic
*Hepatitis B Antibodies: BI, biosynthesis
Hepatitis B Antibodies: BL, blood
*Hepatitis B Surface Antigens: CH, chemistry
*Hepatitis B Surface Antigens: IM, immunology
Mice
Mice, Inbred BALB C
Molecular Sequence Data
Peptide Fragments: IM, immunology
Spleen: CY, cytology
*T-Lymphocytes, Cytotoxic: PH, physiology
Transfection
Tumor Cells, Cultured
CN 0 (Hepatitis B Antibodies); 0 (Hepatitis B Surface Antigens); 0 (Peptide Fragments)

L7 ANSWER 3 OF 112 MEDLINE
AN 95072131 MEDLINE
DN 95072131 PubMed ID: 7981310
TI Cytotoxic T lymphocyte and antibody responses **generated** in rhesus monkeys immunized with retroviral vector-transduced fibroblasts expressing human immunodeficiency virus type-1 IIIB ENV/REV **proteins**.
AU Laube L S; Burrascano M; Dejesus C E; Howard B D; Johnson M A; Lee W T; Lynn A E; Peters G; Ronlov G S; Townsend K S; +
CS Viagene, Inc., San Diego, CA 92121.
SO HUMAN GENE THERAPY, (1994 Jul) 5 (7) 853-62.
Journal code: A12; 9008950. ISSN: 1043-0342.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199501
ED Entered STN: 19950116
Last Updated on STN: 19970203
Entered Medline: 19950103
AB The immune response against human immunodeficiency virus type-1 (HIV-1) is believed to play a role in controlling the early stages of disease progression. The cellular immune response, in particular cytotoxic T lymphocyte (**CTL**) activity, may be important for eliminating virally infected cells in HIV-1-infected individuals. Genetic immunization using retroviral vectors provides an effective means of introducing antigens into the antigen presentation pathways for T cell stimulation. A nonreplicating, amphotropic murine retroviral vector containing the HIV-1 IIIB env gene has been used to transduce primary rhesus monkey fibroblasts for the expression of HIV-1 antigenic determinants. Rhesus monkeys were immunized with four doses of either vector-transduced autologous fibroblasts (VTAF) expressing the HIV-1 IIIB ENV/REV **proteins** or nontransduced autologous fibroblasts (NTAF) administered at 2-week intervals. The animals were evaluated for both the induction of HIV-1-specific immune responses and potential toxicity associated with this ex **vivo** treatment. The VTAF-immunized monkeys **generated CTL** responses specific for HIV-1 ENV/REV expressing autologous target cells, whereas, NTAF-immunized monkeys showed negligible **CTL** activity. The cytotoxic activity was mediated by CD8+, major histocompatibility complex (MHC)-restricted **CTL**. In addition, antibody responses directed against the HIV-1 gp120 **protein** were also detected in the sera of VTAF-immunized monkeys. Clinical and histopathological evaluation of immunized monkeys showed no evidence of significant adverse events. Several animals that received either VTAF or NTAF had detectable anti-cytoplasmic antibodies, but were not positive for anti-nuclear antibodies or rheumatoid factor. Subsequent evaluation of renal, synovial, and hepatic tissue samples from these monkeys revealed no autoimmune disease-associated lesions. This study demonstrates the safety and ability of autologous retroviral vector-transduced cells expressing HIV-1 IIIB ENV/REV **proteins** to stimulate immune responses in a non-human primate model, and provides a basis for this form of genetic immunization in HIV-infected humans.
CT Check Tags: Animal; Comparative Study; Human
*AIDS Vaccines
Antibodies, Antinuclear: AN, analysis
Autoimmune Diseases: ET, etiology
B-Lymphocytes: IM, immunology
Cell Line, Transformed
Cross Reactions
Cytomegalovirus: GE, genetics
Cytoplasm: IM, immunology
*Fibroblasts: IM, immunology
Gene Products, env: GE, genetics
*Gene Products, env: IM, immunology

Gene Products, rev: GE, genetics
*Gene Products, rev: IM, immunology
Genes, Synthetic
*Genetic Vectors
*HIV Antibodies: BI, biosynthesis
HIV-1: GE, genetics
*HIV-1: IM, immunology
Immunization: AE, adverse effects
*Immunization: MT, methods
Liver Diseases: ET, etiology
Macaca mulatta: IM, immunology
Moloney Leukemia Virus: GE, genetics
Recombinant Fusion Proteins: GE, genetics
***Recombinant Fusion Proteins: IM, immunology**
Rheumatoid Factor: AN, analysis
Safety
*T-Lymphocytes, Cytotoxic: IM, immunology
Transduction, Genetic
RN 9009-79-4 (Rheumatoid Factor)
CN 0 (AIDS Vaccines); 0 (Antibodies, Antinuclear); 0 (Gene Products, env); 0 (Gene Products, rev); 0 (Genetic Vectors); 0 (HIV Antibodies); 0 (Recombinant Fusion **Proteins**)
GEN env; gag; pol; rev

L8 ANSWER 3 OF 183 CANCERLIT
AN 1998701207 CANCERLIT
DN 98701207
TI A PHASE I STUDY OF RECOMBINANT VACCINIA **VIRUS** (rV) THAT EXPRESSES **PROSTATE SPECIFIC ANTIGEN** (**PSA**) IN ADULT PATIENTS (pts) WITH ADENOCARCINOMA OF THE PROSTATE (Meeting abstract).
AU Chen A P; Bastian A; Dahut W; Chung Y; Tsang K; Khleif S; Blake K; Gelmann E; Marshall J; Schlom J; Allegra C; Hamilton J M
CS Medicine Branch and Laboratory of Tumor Immunology and Biology, National Cancer Institute, Bethesda, MD; and Vincent T. Lombardi Cancer Center, Washington, DC.
SO Proc Annu Meet Am Soc Clin Oncol, (1998). Vol. 17, pp. A1209.
DT (MEETING ABSTRACTS)
FS ICDB
LA English
EM 199910
AB An rV that expresses human **PSA** (PROSTVAC, Therion Biologic, Cambridge, MA 02142) has shown **immune** responses in rhesus monkeys (Int J Cancer 63(2):231--7, 1995). From 10/16/96 to 10/26/97, 30 pts entered a phase I trial of PROSTVAC. Patients' age range was 49--82 (median 66). All pts had hormone refractory prostate cancer, s/p antiandrogen withdrawal, and prior vaccinia ('smallpox') inoculation. Starting **PSA** ranged from 8.2--3892 ng/ml (median = 83.2). Four cohorts of patients received PROSTVAC q 4 wk [times] 3 at 2.65 [times] 10[Superscript 5] (n = 8) or 2.65 [times] 10[Superscript 6] (n = 7) plaque forming units (PFU) by dermal scarification (DS) or at 2.65 [times] 10[Superscript 6](n = 6) or 2.65 [times] 10[Superscript 8] (n = 9) PFU given SQ. Treatment was limited to 3 vaccinations with re-staging 4 wks after the last vaccination. Five of 8, 5/7, 3/6 and 3/9 pts at each dose level completed all three vaccinations. Pts did not complete three vaccinations due to PD (7), second primary (1), & patient refusal (1) and 5 are still under treatment. All patients had a positive reaction with local erythema at the vaccination site with no or mild symptoms of fever, fatigue, and malaise. Local and skin reactions were less in the SQ vs. DS group. Drug related hematologic, renal, and liver function toxicities were grade 0-1. After three vaccinations, 4 pts had stable disease, and 10 had PD. Two pts are too early to evaluate. Of the 4 pts with stable disease at the end of treatment, 2 have progressed at 5 & 6 months. Recombinant vaccinia **virus** can be safely administered and can serve as a **vector** for repeated exposures to a gene product. Immunologic assessment of these patients is pending. (C) American Society of Clinical Oncology 1998.

L8 ANSWER 4 OF 183 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1998:294281 BIOSIS
DN PREV199800294281
TI Anti-**PSA immune** responses induced by **viral vector immunization**: A model for immunotherapy of prostate cancer.
AU Lubaroff, David M.; Elzey, Bennett D.; Ratliff, Timothy L.
CS Iowa City, IA USA
SO Journal of Urology, (May, 1998) Vol. 159, No. 5 SUPPL., pp. 9. Meeting Info.: 93rd Annual Meeting of the American Urological Association, Inc. San Diego, California, USA May 30-June 4, 1998 American Urological Association
. ISSN: 0022-5347.
DT Conference
LA English
CC Neoplasms and Neoplastic Agents - General *24002
Cytology and Cytochemistry - General *02502
Pathology, General and Miscellaneous - Therapy *12512
Urinary System and External Secretions - General; Methods *15501

Reproductive System - General; Methods *16501
Virology - General; Methods *33502
Immunology and Immunochemistry - General; Methods *34502
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
BC Adenoviridae 02601
Poxviridae 02621
Muridae 86375
IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); Tumor Biology
IT Diseases
prostate cancer: neoplastic disease, reproductive system disease/male, urologic disease
IT Chemicals & Biochemicals
prostate specific antigen
IT Methods & Equipment
immunotherapy: immunological method, therapeutic method
IT Miscellaneous Descriptors
anti-**PSA immune** response [anti-**prostate specific antigen immune** response]: model, **viral vector immunization**; Meeting Abstract
ORGN Super Taxa
Adenoviridae: Animal **Viruses**, **Viruses**, Microorganisms; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Poxviridae: Animal **Viruses**, **Viruses**, Microorganisms
ORGN Organism Name
adenovirus type 5 (Adenoviridae); mouse (Muridae): Balb/c, model; vaccinia **virus** (Poxviridae); P815 (Muridae): murine cells
ORGN Organism Superterms
Animal **Viruses**; Animals; Chordates; Mammals; Microorganisms; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates; **Viruses**

L8 ANSWER 5 OF 183 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1998:193947 BIOSIS
DN PREV199800193947
TI Immunotherapy of prostate cancer: Anti-**PSA** cytotoxic lymphocytes induced by **viral vector immunization**.
AU Lubaroff, D. M. (1); Elzey, B. D.; Ratliff, T. L.
CS (1) Univ. Iowa, Iowa City, IA 52242 USA
SO Proceedings of the American Association for Cancer Research Annual Meeting, (March, 1998) Vol. 39, pp. 11.
Meeting Info.: 89th Annual Meeting of the American Association for Cancer Research New Orleans, Louisiana, USA March 28-April 1, 1998 American Association for Cancer Research
. ISSN: 0197-016X.
DT Conference
LA English
CC Neoplasms and Neoplastic Agents - Immunology *24003
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
BC Muridae 86375
IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); Tumor Biology
IT Diseases
prostate cancer: immunotherapy, neoplastic disease, reproductive system disease/male, urologic disease
IT Chemicals & Biochemicals

PSA [prostate specific antigen]

IT Methods & Equipment
anti-**PSA** cytotoxic T lymphocyte induction: immunotherapy, therapeutic method; **viral vector immunization: immunization** method

IT Miscellaneous Descriptors
Meeting Abstract

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
mouse (Muridae): strain-BALB/c

ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L8 ANSWER 9 OF 183 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1995:333982 BIOSIS
DN PREV199598348282
TI Use of recombinant **prostate-specific antigen** for immunoassay calibration.
AU Ng, Phillip C. (1); Zhou, Zeqi; Very, Donald L.; Allard, W. Jeffrey; Barnett, Thomas R.; Yeung, Kwok K.
CS (1) Miles Diagnostics, Tarrytown, NY 10591 USA
SO Clinical Chemistry, (1995) Vol. 41, No. S6 PART 2, pp. S218.
Meeting Info.: 47th Annual Meeting of the American Association for Clinical Chemistry, Inc. Anaheim, California, USA July 16-20, 1995
ISSN: 0009-9147.
DT Conference
LA English
CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
Cytology and Cytochemistry - Animal *02506
Genetics and Cytogenetics - Human *03508
Clinical Biochemistry; General Methods and Applications *10006
Biochemical Methods - Proteins, Peptides and Amino Acids *10054
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Enzymes - Methods *10804
Reproductive System - Physiology and Biochemistry *16504
Neoplasms and Neoplastic Agents - Immunology *24003
Neoplasms and Neoplastic Agents - Biochemistry *24006
Genetics of Bacteria and Viruses *31500
Immunology and Immunochemistry - General; Methods *34502
Invertebrata, Comparative and Experimental Morphology, Physiology and Pathology - Insecta - General *64072
BC Baculoviridae 02603
Insecta - Unspecified 75300
Hominidae *86215
IT Major Concepts
Cell Biology; Clinical Chemistry (Allied Medical Sciences); Enzymology (Biochemistry and Molecular Biophysics); Genetics; **Immune** System (Chemical Coordination and Homeostasis); Methods and Techniques; Oncology (Human Medicine, Medical Sciences); Reproductive System (Reproduction)
IT Chemicals & Biochemicals
SERINE PROTEASE
IT Miscellaneous Descriptors
BACULOVIRUS **VECTOR**; IMMUNOLOGIC METHOD; INSECT CELLS; MEETING ABSTRACT; **PROSTATE SPECIFIC ANTIGEN** GENE; SERINE PROTEASE; TUMOR MARKER
ORGN Super Taxa
Baculoviridae: **Viruses**; Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Insecta - Unspecified: Insecta, Arthropoda, Invertebrata, Animalia
ORGN Organism Name

human (Hominidae); Baculoviridae (Baculoviridae); Insecta (Insecta - Unspecified)

ORGN Organism Superterms
animals; arthropods; chordates; humans; insects; invertebrates; mammals; microorganisms; primates; vertebrates; **viruses**

RN 37259-58-8 (SERINE PROTEASE)

=>

1: Int J Cancer 1995 Oct 9;63(2):231-7

A recombinant vaccinia virus expressing human prostate-specific antigen (PSA): safety and immunogenicity in a non-human primate.

Hodge JW, Schlom J, Donohue SJ, Tomaszewski JE, Wheeler CW, Levine BS, Gritz L, Panicali D, Kantor JA.

Laboratory of Tumor Immunology and Biology, National Cancer Institute, Bethesda, MD 20892, USA.

Prostate-specific antigen (PSA) is a serine protease secreted by prostatic epithelial cells and is widely used as a marker for prostate cancer. The tissue specificity of PSA makes it a potential target for active specific immunotherapy, especially in prostate cancer patients who have undergone prostatectomy and in whom the only PSA-expressing tissue in the body resides in metastatic deposits. We report here the cloning, construction and immunological consequences of immunization of rhesus monkeys with a recombinant vaccinia virus expressing human PSA (designated rV-PSA). The prostate gland of the rhesus is structurally and functionally similar to the human prostate. While rodent and other mammalian species do not share homology with human PSA, there is 94% homology between the amino acid sequences of rhesus and human PSA. Immunization of rhesus monkeys with wild-type vaccinia virus or rV-PSA elicited the usual low-grade constitutional symptoms of vaccinia virus infection. There was no evidence of any adverse effects in any immunized monkeys. A short-lived PSA-specific IgM antibody response was noted in all rV-PSA immunized monkeys regardless of dose level. All monkeys receiving the 10(8)pfu dose of rV-PSA demonstrated PSA-specific T-cell responses that were maintained up to 270 days. No differences in anti-PSA immune responses or toxicity were observed in animals that received prostatectomy prior to immunization. Our results thus demonstrate the safety and immunogenicity of rV-PSA in a non-human primate and have implications for potential specific immunotherapy protocols using PSA as a target.

PMID: 7591210 [PubMed - indexed for MEDLINE]

Display | Abstract | Sort | Save | Text | Clip Add | Order

=> d l22 2,6,15,11,24 all

L22 ANSWER 2 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 94181759 EMBASE
DN 1994181759
TI Induction of a cytotoxic T cell response by co-injection of a T helper peptide and a cytotoxic T lymphocyte peptide in incomplete Freund's adjuvant (IFA): Further enhancement by pre-injection of IFA alone.
AU Valmori D.; Romero J.F.; Men Y.; Maryanski J.L.; Romero P.; Corradin G.
CS Institute of Biochemistry, University of Lausanne,CH-1066 Epalinges, Switzerland
SO European Journal of Immunology, (1994) 24/6 (1458-1462).
ISSN: 0014-2980 CODEN: EJIMAF
CY Germany
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
LA English
SL English
AB We have previously demonstrated that it is possible to induce a consistent and strong cytolytic T lymphocyte (**CTL**) response to synthetic peptides, corresponding to poorly immunogenic malaria **CTL** epitopes, by co-injecting them with peptides representing defined T helper (Th) epitopes in incomplete Freund's adjuvant (IFA). In this study we have tested different immunization protocols to improve further the elicitation of the **CTL** response. We show that the **CTL** response to a mixture of Th + **CTL** peptides **administered** in IFA was further enhanced by a previous injection of the Th epitope peptide in IFA. Moreover, we found that the response could be significantly augmented by a pre-injection of IFA alone. This enhancement was observed only if the Th epitope was also present in the second injection. The number of lymph node cells recovered was 2-3-fold higher in mice pre-injected with IFA, but the increase in specific **CTL** activity, expressed as lytic units per animal, by pre-injection of IFA was at least 10-20-fold. Thus, pre-injection of IFA clearly increases the magnitude of a subsequent **CTL** response.
CT Medical Descriptors:
*cytotoxic t lymphocyte
animal cell
animal experiment
article
cellular immunity
controlled study
female
helper cell
immunization
lymph node cell
malaria
mouse
nonhuman
priority journal
Drug Descriptors:
cell protein
epitope: EC, endogenous compound
freund adjuvant
RN (freund adjuvant) 9007-81-2

L22 ANSWER 6 OF 24 MEDLINE DUPLICATE 4
AN 95072131 MEDLINE
DN 95072131 PubMed ID: 7981310
TI Cytotoxic T lymphocyte and antibody responses generated in rhesus monkeys immunized with retroviral vector-transduced fibroblasts expressing human immunodeficiency virus type-1 IIIB ENV/REV **proteins**.
AU Laube L S; Burrascano M; Dejesus C E; Howard B D; Johnson M A; Lee W T; Lynn A E; Peters G; Ronlov G S; Townsend K S; +

CS Viagene, Inc., San Diego, CA 92121.
SO HUMAN GENE THERAPY, (1994 Jul) 5 (7) 853-62.
Journal code: A12; 9008950. ISSN: 1043-0342.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199501
ED Entered STN: 19950116
Last Updated on STN: 19970203
Entered Medline: 19950103
AB The immune response against human immunodeficiency virus type-1 (HIV-1) is believed to play a role in controlling the early stages of disease progression. The cellular immune response, in particular cytotoxic T lymphocyte (**CTL**) activity, may be important for eliminating virally infected cells in HIV-1-infected individuals. Genetic immunization using retroviral vectors provides an effective means of introducing antigens into the antigen presentation pathways for T cell stimulation. A nonreplicating, amphotropic murine retroviral vector containing the HIV-1 IIIB env gene has been used to transduce primary rhesus monkey fibroblasts for the expression of HIV-1 antigenic determinants. Rhesus monkeys were immunized with four doses of either vector-transduced autologous fibroblasts (VTAF) expressing the HIV-1 IIIB ENV/REV **proteins** or nontransduced autologous fibroblasts (NTAF) **administered** at 2-week intervals. The animals were evaluated for both the induction of HIV-1-specific immune responses and potential toxicity associated with this ex vivo treatment. The VTAF-immunized monkeys generated **CTL** responses specific for HIV-1 ENV/REV expressing autologous target cells, whereas, NTAF-immunized monkeys showed negligible **CTL** activity. The cytotoxic activity was mediated by CD8+, major histocompatibility complex (MHC)-restricted **CTL**. In addition, antibody responses directed against the HIV-1 gp120 **protein** were also detected in the sera of VTAF-immunized monkeys. Clinical and histopathological evaluation of immunized monkeys showed no evidence of significant adverse events. Several animals that received either VTAF or NTAF had detectable anti-cytoplasmic antibodies, but were not positive for anti-nuclear antibodies or rheumatoid factor. Subsequent evaluation of renal, synovial, and hepatic tissue samples from these monkeys revealed no autoimmune disease-associated lesions. This study demonstrates the safety and ability of autologous retroviral vector-transduced cells expressing HIV-1 IIIB ENV/REV **proteins** to stimulate immune responses in a non-human primate model, and provides a basis for this form of genetic immunization in HIV-infected humans.
CT Check Tags: Animal; Comparative Study; Human
*AIDS Vaccines
Antibodies, Antinuclear: AN, analysis
Autoimmune Diseases: ET, etiology
B-Lymphocytes: IM, immunology
Cell Line, Transformed
Cross Reactions
Cytomegalovirus: GE, genetics
Cytoplasm: IM, immunology
*Fibroblasts: IM, immunology
Gene Products, env: GE, genetics
*Gene Products, env: IM, immunology
Gene Products, rev: GE, genetics
*Gene Products, rev: IM, immunology
Genes, Synthetic
*Genetic Vectors
*HIV Antibodies: BI, biosynthesis
HIV-1: GE, genetics
*HIV-1: IM, immunology
Immunization: AE, adverse effects
*Immunization: MT, methods

Liver Diseases: ET, etiology
Macaca mulatta: IM, immunology
Moloney Leukemia Virus: GE, genetics
Recombinant Fusion Proteins: GE, genetics
***Recombinant Fusion Proteins: IM, immunology**
Rheumatoid Factor: AN, analysis
Safety
*T-Lymphocytes, Cytotoxic: IM, immunology
Transduction, Genetic
RN 9009-79-4 (Rheumatoid Factor)
CN 0 (AIDS Vaccines); 0 (Antibodies, Antinuclear); 0 (Gene Products, env); 0 (Gene Products, rev); 0 (Genetic Vectors); 0 (HIV Antibodies); 0 (Recombinant Fusion **Proteins**)
GEN env; gag; pol; rev

L22 ANSWER 15 OF 24 MEDLINE DUPLICATE 10
AN 92166401 MEDLINE
DN 92166401 PubMed ID: 1538138
TI In vivo cytotoxic T lymphocyte induction with soluble **proteins administered** in liposomes.
AU Reddy R; Zhou F; Nair S; Huang L; Rouse B T
CS Department of Microbiology, College of Veterinary Medicine, University of Tennessee, Knoxville 37996-0845.
NC AI24762 (NIAID)
CA24553 (NCI)
SO JOURNAL OF IMMUNOLOGY, (1992 Mar 1) 148 (5) 1585-9.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199203
ED Entered STN: 19920417
Last Updated on STN: 19920417
Entered Medline: 19920330
AB The in vivo induction of a **CTL** response usually requires that Ag be endogenously synthesized so that appropriate processing can occur. In most of the few examples where successful **CTL** induction was reported with **proteins** and peptides, unacceptable adjuvants or means of Ag formulation were used. In the present report, liposomes were used to incorporate the soluble **proteins** OVA and beta-galactosidase. This simple and convenient to use approach, which requires minimal amounts of Ag, results in priming for a CD8+ **CTL** response and the establishment of immunologic memory. The liposome approach may not only prove a convenient means of inducing **CTL** responses in vivo but may also be useful to study the mechanisms of Ag processing.
CT Check Tags: Animal; Female; Support, U.S. Gov't, P.H.S.
Antigens, CD8: AN, analysis
Liposomes: AD, administration & dosage
Mice
Mice, Inbred BALB C
Mice, Inbred C57BL
*Ovalbumin: AD, administration & dosage
Ovalbumin: IM, immunology
*T-Lymphocytes, Cytotoxic: PH, physiology
*beta-Galactosidase: AD, administration & dosage
beta-Galactosidase: IM, immunology
RN 9006-59-1 (Ovalbumin)
CN 0 (Antigens, CD8); 0 (Liposomes); EC 3.2.1.23 (beta-Galactosidase)

L22 ANSWER 11 OF 24 MEDLINE DUPLICATE 8
AN 93341015 MEDLINE
DN 93341015 PubMed ID: 8340941

TI Cytotoxic T-cell response and in vivo protection against tumor cells harboring activated ras proto-oncogenes.

CM Comment in: J Natl Cancer Inst. 1993 Aug 18;85(16):1266-8

AU Fenton R G; Taub D D; Kwak L W; Smith M R; Longo D L

CS Clinical Research Branch, National Cancer Institute-Frederick Cancer Research and Development Center, Frederick, Md 21702-1201.

SO JOURNAL OF THE NATIONAL CANCER INSTITUTE, (1993 Aug 18) 85 (16) 1294-302. Journal code: J9J; 7503089. ISSN: 0027-8874.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199308

ED Entered STN: 19930917
Last Updated on STN: 20000303
Entered Medline: 19930831

AB BACKGROUND: Activated forms of the ras proto-oncogene have been found in approximately 30% of human malignancies, including pancreatic, colon, and lung adenocarcinomas. Ras oncoproteins arise by somatic mutation and contain amino acid changes at residues 12, 13, or 61, thus generating unique tumor specific **proteins** that are attractive targets for cancer therapy. PURPOSE: The goal of this study was to determine whether vaccination with mutant Ras **protein** could lead to the generation of cytotoxic T lymphocytes (**CTLs**) specific for the mutant epitope and to protection against challenge with tumor cells expressing the mutant oncoprotein. METHODS: To determine a methodology for generating **CTL** responses following immunization with soluble **protein**, ovalbumin was used as a model tumor antigen. C57BL/6 mice were immunized with soluble ovalbumin **administered** intraperitoneally at 2-week intervals or with intravenous injection of ovalbumin or osmotically loaded splenocytes. Immunized mice were challenged with E.G7 cells (which express a transfected ovalbumin gene), and tumor growth was monitored. Generation of ovalbumin-specific **CTLs** was determined by 51Cr release assays. Purified wild-type or mutant H-Ras **proteins** (containing single amino acid substitutions at position 12 converting Gly to Arg or Val) were used to immunize BALB/c mice intraperitoneally. Ras-immunized mice were challenged with tumor cells containing Arg 12 or Val 12 mutations or not harboring mutant forms of Ras. Cytolytic and proliferative responses to mutant forms of Ras were studied, and the effects of in vivo depletion of CD4+ or CD8+ T lymphocytes were determined. RESULTS: In vivo challenge with E.G7 showed that intraperitoneal immunization with soluble ovalbumin was as effective as osmotic loading, resulting in long-term disease-free survival of some mice and the development of ovalbumin-specific **CTLs**. Immunization with Arg 12 Ras led to disease-free survival in nine of 10 animals challenged with tumor cells containing an Arg 12 mutation, while no protection was afforded against tumors expressing other forms of Ras or other oncogenes. Splenocytes from BALB/c mice immunized with Arg 12 Ras demonstrated cytolytic activity specific against tumor cells expressing Arg 12 Ras, with most of this activity residing in the CD8+ subset. Mutation-specific proliferation to Arg 12 Ras peptides was also observed. Immunization with Val 12 Ras did not elicit detectable Val 12-specific immunity. CONCLUSIONS: Antigen-specific **CTLs** can be induced following intraperitoneal immunization of mice with purified, soluble **proteins**. For both ovalbumin and Arg 12 Ras, specific in vivo protection against tumor cell challenge was observed.

CT Check Tags: Animal; Female
Amino Acid Sequence
Gene Expression Regulation, Neoplastic
Mice
Mice, Inbred BALB C
Mice, Inbred C57BL
Molecular Sequence Data
Mutation

*Neoplasms, Experimental: IM, immunology
Neoplasms, Experimental: PC, prevention & control
Ovalbumin: IM, immunology
Proto-Oncogene Protein p21(ras): GE, genetics
***Proto-Oncogene Protein p21(ras): IM, immunology**
*T-Lymphocytes, Cytotoxic: IM, immunology
Tumor Cells, Cultured
Vaccination
RN 9006-59-1 (Ovalbumin)
CN EC 3.6.1.- (Proto-Oncogene **Protein** p21(ras))

L22 ANSWER 24 OF 24 CANCERLIT
AN 86627030 CANCERLIT
DN 86627030
TI IN VITRO AND IN VIVO STIMULATION OF MURINE LYMPHOCYTES BY HUMAN RECOMBINANT INTERLEUKIN 2.
AU Talmadge J E; Dennis-Tait S; Schneider M E; Meeker A K; Adams J S; Ortaldo J R; Wiltrout R H
CS Preclinical Screening Lab., Program Resources, Inc., NCI-FCRF, Frederick, MD.
SO Non-serial, (1985). Immunity to Cancer. Reif AE, Mitchell MS, eds. New York, Academic Press.
DT (MEETING PAPER)
FS ICDB
LA English
EM 198612
AB The immunomodulatory effect of human interleukin 2 (IL-2) on mouse cells was studied both in vitro and in vivo. The ability of recombinant IL-2 (rIL-2) **protein** to stimulate murine T-cell activity in vitro was assessed in an allogeneic mixed lymphocyte response (MLR) assay. The addition of rIL-2 to the MLR increased the allogeneic proliferation response in a dose-dependent manner. Furthermore, the addition of rIL-2 to responder cells cultured in the absence of stimulator cells was blastogenic. Similar results were observed using human peripheral blood lymphocytes in which both the baseline proliferation and the MLR were stimulated by rIL-2. The rIL-2 also acted as an adjuvant for varying amounts of tumor vaccines composed of MBL-2 tumor cells. Suboptimal amounts of irradiated MBL-2 lymphoma vaccines induced low, but significant, levels of specific cytotoxic T lymphocytes (**CTL**) in the peritoneum, but not in the spleen, following ip injection. When mice were vaccinated ip with MBL-2 together with IL-2 (**administered** twice a day on the day of vaccination as well as the following 3 days), high rIL-2 doses inhibited the development of cytotoxic cells whereas lower doses stimulated **CTL** activity. Human rIL-2 had significant ability to augment natural killer cell activity for murine lymphocytes, and also to stimulate by itself significant proliferation of both mouse and human lymphocytes. This was observed in the absence of any additional exogenous maturational signal such as alloantigen, non-IL-2 lymphokines, mitogens, or heterologous serum. This does not preclude a role for other lymphokines induced by rIL-2, which may augment the maturation of lymphocytes or increase the number of IL-2 receptors. (8 Refs)
CN **0 (Recombinant Proteins)**

WEST

End of Result Set

☐ Generate Collection Print

L1: Entry 1 of 1 File: USPT Dec 26, 2000

US-PAT-NO: 6165460
DOCUMENT-IDENTIFIER: US 6165460 A

TITLE: Generation of immune responses to prostate-specific antigen (PSA)

DATE-ISSUED: December 26, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schlom; Jeffrey	Potomac	MD		
Panicali; Dennis L.	Acton	MA		

US-CL-CURRENT: 424/93.2; 424/204.1, 424/232.1, 424/277.1, 424/93.1, 424/93.3, 424/93.6, 435/320.1

CLAIMS:

What is claimed is:

1. A method for generating an immune response to prostate-specific antigen (PSA) comprising, introducing a sufficient amount of a first pox virus vector to a host to stimulate an immune response, wherein the pox virus vector has at least one insertion site containing a DNA segment encoding PSA operably linked to a promoter capable of expression in the host.

2. The method of claim 1, further comprising at at least one periodic interval after introduction of the first pox virus vector contacting the host with additional PSA or a cytotoxic T-cell eliciting epitope thereof.

3. The method of claim 2, wherein the host is contacted with the additional PSA by introducing a second pox virus vector to the host having at least one insertion site containing a DNA segment encoding the PSA operably linked to a promoter capable of expression in the host.

4. A method for generating an immune response to prostate-specific antigen (PSA) in a host, comprising:

a. contacting the host with a sufficient amount of PSA or a cytotoxic T-cell eliciting epitope thereof; and

b. at least one periodic interval thereafter contacting the host with additional PSA or a cytotoxic T-cell eliciting epitope thereof.

5. The method of claim 4, wherein the host is contacted with the additional PSA by introducing a pox virus vector to the host having at least one insertion site containing a DNA segment encoding PSA or a cytotoxic T-cell eliciting epitope thereof operably linked to a promoter capable of expression in the host.

6. The method of claim 1 or 5, wherein the pox virus is selected from the group of pox viruses consisting of suipox, avipox, capripox and orthopox virus.

7. The method of claim 6, wherein the orthopox virus is vaccinia.

8. The method of claim 7, wherein the avipox is fowlpox, canary pox and pigeon pox.

9. The method of claim 8, wherein the suipox is swinepox.

10. The method of claim 3, wherein the first pox virus vector is vaccinia and the second pox virus vector is selected from the group of pox viruses consisting of suipox, avipox, capripox and orthopox virus.

11. The method of claim 2 or 4, wherein the PSA or T-cell eliciting epitope is formulated with an adjuvant or is in a liposomal formulation.

12. The method of claim 11, wherein the adjuvant is selected from the group consisting of RIBI Detox, QS21 and incomplete Freund's adjuvant.

13. A method for generating an immune response to PSA comprising contacting a host with a cytotoxic T-cell eliciting epitope of PSA.

14. The method of claim 13, wherein the T-cell eliciting epitope is formulated with an adjuvant or is in a liposomal formulation.

15. The method of claim 12, wherein the adjuvant is selected from the group consisting of RIBI Detox, QS21 and incomplete Freund's adjuvant.

16. A pharmaceutical composition comprising a pox virus vector having at least one insertion site containing a DNA segment encoding PSA operably linked to a promoter and a pharmaceutical carrier.

17. The method of claim 3, wherein the second pox virus vector is from a different genus than the first pox virus vector.

WEST

Help | Logout | Interrupt

Main Menu | Search Form | Posting Counts | Show S Numbers | Edit S Numbers | Preferences | Cases

Search Results -

Terms	Documents
6165460.pn.	1

Database: US Patents Full-Text Database
US Pre-Grant Publication Full-Text Database
JPO Abstracts Database
EPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: L1 and B7

Refine Search

Recall Text | Clear

Search History

DATE: Tuesday, March 18, 2003 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT; PLUR=YES; OP=OR			
L4	6165460.pn.	1	L4
L3	5833975.pn.	1	L3
L2	5833975	13	L2
DB=EPAB; PLUR=YES; OP=OR			
L1	wo009219266a1	1	L1

END OF SEARCH HISTORY

1: Cancer Res 1995 Aug 15;55(16):3598-603 Related Articles, Link

Admixture of a recombinant vaccinia virus containing the gene for the costimulatory molecule B7 and a recombinant vaccinia virus containing a tumor-associated antigen gene results in enhanced specific T-cell responses and antitumor immunity.

Hodge JW, McLaughlin JP, Abrams SI, Shupert WL, Schlom J, Kantor JA.

Laboratory of Tumor Immunology and Biology, National Cancer Institute, NIH, Bethesda, Maryland 20892, USA.

At least two signals are required for the activation of naive T cells by antigen-bearing target cells: an antigen-specific signal, delivered through the T-cell receptor, and a costimulatory signal delivered through the T-cell surface molecule CD28 by its natural ligand B7-1. The immunological benefit of coexpression of B7 with target antigen has been demonstrated with the use of several retroviral systems to transfect antigen-bearing cells. Although engineering recombinant constructs with genes for two or more antigens can mediate the dual expression of those antigens, disadvantages of this approach include the time for construction of each desirable combination and the inability to control differential expression levels of each gene product. An alternative approach would utilize separate constructs that could be admixed appropriately before administration. In this report we describe the functional consequences of the admixture of recombinant vaccinia murine B7-1 (rV-B7) to recombinant vaccinia expressing the human carcinoembryonic antigen gene (rV-CEA). Coinfection of cells resulted in high levels of cell surface expression of both the CEA and B7 molecules. Immunization of mice with various ratios (1:3, 1:1, 3:1) of rV-CEA and rV-B7 demonstrated that an admixture of rV-CEA and rV-B7 at a 3:1 ratio resulted in the generation of optimal CEA-specific T-cell responses. Next, we examined the efficacy of this admixture on antitumor activity. Typically, injection of murine carcinoma cells expressing CEA leads to the death of the host. One immunization of C57BL/6 mice with rV-CEA:rV-B7 (3:1) resulted in no tumor establishment. In contrast, administration of rV-CEA or rV-B7 alone had little or no antitumor effects. These studies demonstrate the advantages of the use of recombinant vaccinia viruses to deliver B7 molecules in combination with a tumor-associated antigen. The availability

of the rV-B7 single construct and the ability to alter the B7 ratio could also have potential utility when coinfecting rV-B7 with recombinant vaccinia viruses containing genes for infectious agents or other tumor-associated antigen genes.

PMID: 7543017 [PubMed - indexed for MEDLINE]

1: Cancer 1996 May 1;77(9):1862-72

Related Articles, Link

In vitro modulation of tumor progression-associated properties of hormone refractory prostate carcinoma cell lines by cytokines.

Sokoloff MH, Tso CL, Kaboo R, Taneja S, Pang S, deKernion JB, Belldegrun AS.

Immunotherapy Laboratory, Prostate Cancer Program, Division of Urology, Department of Surgery, UCLA School of Medicine, Los Angeles, California 90024, USA.

BACKGROUND: Cytokines exert cytostatic and immunomodulatory effects on carcinoma cells. Growth inhibition of human prostate carcinoma by cytokines has been demonstrated both in vitro and in vivo, whereas the cellular and molecular changes in prostate carcinoma properties after cytokine treatment have never been characterized. We have thus investigated whether the intrinsic properties of prostate carcinoma cells that are associatec with tumor development and progression can be altered by direct cytokine treatment. METHODS: LNCaP, DU-145, and PC-3 cell lines were treated with tumor necrosis factor-alpha (TNF-alpha) (200 U/mL), interferon-gamm: (IFN-gamma) (500 U/mL), human leukocyte interferon (IFN-alpha) (500 U/mL), and interleukin-2 (IL-2) (400 U/mL). The expression of (prostate-specific antigen [PSA] and prostate-specific membrane [PSM]), androgen receptor (AR), growth factors, oncogenes, collagenase, cell adhesion molecules, HLA antigens, cell adhesion to human bone marrow stroma, and cell growth were determined by quantitative polymerase chain reaction (PCR) analysis, fluorescence-activated cell sorter (FACS) analysis, and cell attachment and proliferation assays, and were compared with non-treated cells. RESULTS: PCR analysis indicated that only LNCaP cells expressed PSA, PSM, and AR mRNA. Cytokine treatment did not alter PSM mRNA expression, whereas a 15-fold decrease in PSA and a 5-fold reduction in AR mRNA expression was detected in TNF-alpha-treated cells. The down regulation of PSA production was also demonstrated at the protein level in a dose-dependent fashion. A fivefold decrease in PSA mRNA was also detected in IL-2-treated LNCaP cells but without a reduction in AR. Down regulated epidermal growth factor receptor (EGF-R) and basic fibroblast growth factor (b-FGF) mRNA expressions were detected in TNF-alpha- and IFN-alpha-treated DU-145 and PC-3 cells, whereas, only reduced EGF-R

expression was observed in LNCaP cells. IFN-gamma and IL-2 treatment down regulated the expression of collagenase Type IV mRNA in DU-145 and PC-3 cells, whereas tumor transforming growth factor-beta (TGF-beta) and IL-6 mRNA expressions did not exhibit any essential changes after cytokine treatment. A reduction in c-myc mRNA expression was observed in TNF-alpha- and IFN-alpha-treated cells, whereas no change in HER-2 expression was noted in any cytokine treated cells. Up regulated P-cadherin, but not E-cadherin, mRNA expression was detected in TNF-alpha- and IFN-gamma-treated PC-3 cells. FACS analysis revealed that all but IL-2-treated cells had enhanced HLA Class I expression, with the maximum effect seen ir TNF-alpha-treated LNCaP cells (threefold increase). Up regulated HLA Class II expression was seen only in IFN-gamma-treated cells. All cytokine-treated DU-145 and PC-3 cells expressed reduced levels of alpha3, but not beta1, integrin. Up regulated of ICAM-1 expression was seen in all cytokine treated DU-145 and PC-3 cells, whereas no change in CD44 occurred. Cytokine treatment reduced the binding affinity of LNCaP and DU-145, but not of PC-3 cells, to human bone marrow stromal cells, and all cytokines but IL-2 showed a mild to moderate growth inhibition to prostate cancer cells, with a marked inhibition only observed in TNF-alpha-treated LNCaP cells. CONCLUSIONS: Cytokine treatment can effectively alter several prostate carcinoma properties that are closely associated with tumor invasion and a metastatic phenotype, suggesting that immunotherapy via the local delivery of cytokines may have a potentially therapeutic role in the treatment of hormone-refractory prostate cancer through both direct and indirect antitumor mechanisms.

PMID: 8646686 [PubMed - indexed for MEDLINE]

1: J Natl Cancer Inst 1992 Jul 15;84(14):1084-91 Related Articles, Link

Comment in:
- J Natl Cancer Inst. 1992 Jul 15;84(14):1059-61.

Antitumor activity and immune responses induced by a recombinant carcinoembryonic antigen-vaccinia virus vaccine.

Kantor J, Irvine K, Abrams S, Kaufman H, DiPietro J, Schlom J.

Laboratory of Tumor Immunology and Biology, National Cancer Institute, Bethesda, Md 20892.

BACKGROUND: Human carcinoembryonic antigen (CEA) is a 180-kd glycoprotein expressed in human colorectal, gastric, pancreatic, breast, and non-small-cell lung carcinomas. Previous studies have demonstrated enhanced immune responses to other antigens presented with vaccinia virus proteins via a recombinant vaccinia virus construct. In addition, we have developed a recombinant CEA-vaccinia virus construct, designated rV(WR)-CEA, and have demonstrated humoral anti-CEA responses in mice after immunization with that virus. PURPOSE: The goals of this study were (a) to construct a recombinant CEA-vaccinia vaccine in a less virulent vaccinia strain that is potentially safe and effective for treatment of patients whose tumors express CEA and (b) to evaluate the ability of the recombinant CEA-vaccinia vaccine to prevent and reverse tumor growth in mice and to elicit cell-mediated and humoral anti-CEA immune responses. METHODS: Using the New York City strain of vaccinia virus, which is used in smallpox vaccination and is more attenuated for humans than rV(WR), we derived a recombinant CEA-vaccinia construct, designated rV(NYC)-CEA. The ability of this construct to induce antitumor immunity was evaluated in mice receiving subcutaneous injections of murine colon adenocarcinoma cells expressing the human CEA gene. RESULTS: Administration of rV(NYC)-CEA in mice induced strong anti-CEA antibody responses, as well as CEA-specific cell-mediated responses, including delayed-type hypersensitivity, lymphoproliferative, and cytotoxic responses. Vaccination of mice with the rV(NYC)-CEA rendered them resistant to the growth of subsequently transplanted CEA-expressing tumors. Moreover, when mice were vaccinated 7 days after tumor cell injection, tumor growth was either greatly reduced or eliminated. No toxic effects were observed in any of the mice. CONCLUSION: These studies demonstrate that antitumor activity can be

induced with the use of a recombinant CEA-vaccinia virus construct derived from an attenuated vaccinia strain, and they reveal the range of cell-mediated and humoral responses induced by this recombinant vaccine.

PMID: 1619682 [PubMed - indexed for MEDLINE]
